

## REMARKS

### REMARKS REGARDING NOTICE OF NON-COMPLIANT

#### AMENDMENT:

This is in response to the Notice of Non-Compliant Amendment dated February 27, 2006.

The Notice states, by checkmark in the appropriate box, that “the listing of claims does not include all pending claims (including withdrawn claims).”

Applicant respectfully submits that this box was marked in error. The application was originally filed with 34 claims. There has been no requirement for restriction/election of species and no claim has been withdrawn from consideration. (see the Office Action of November 4, 2005).

In the amendment filed on February 4, 2006 (with certificate of mailing) Claims 1- 9 and 28 – 32 were canceled. This is clearly indicated in the “Complete Listing of Pending Claims”. Because these claims were canceled, and not “withdrawn from consideration”, the rules do not require the reproduction of their text.

Each claim, except, Claim 34, has a proper identifier, such as “original” or “presently amended”. The lack of the proper identifier as “original” of Claim 34 has been *corrected* in the present corrected amendment. The undersigned attorney regrets this previous oversight.

The Notice of Non-Compliant Amendment states that “Claim 34 has no text”. This is respectfully submitted to be in error. Claim 34 is a dependent claim that refers back to Claim 33. Claim 34 adds to the text of Claim 33 by

stating that the composition described in Claim 33 is “adapted for topical administration to a human being”.

In the present response applicant, acting through the undersigned attorney, reproduces the remarks which were submitted on February 4, 2006 in response to the Office Action of November 4, 2005. However, the voluminous associated documents (such as terminal disclaimers) are not resubmitted because these were previously sent to the Patent Office with appropriate Certificates of Mailing.

ORIGINALLY SUBMITTED REMARKS IN RESPONSE TO THE  
OFFICE ACTION OF NOVEMBER 4, 2005

The obviousness type double patenting rejection were overcome by  
concurrent filing of the appropriate terminal disclaimers

The obviousness type double patenting rejection invoked issued copending application serial number 10/389071 and United States Patent No. 6,740,676. Terminal disclaimers regarding these two references are filed concurrently with the present response, thereby overcoming these grounds of rejection.

Rejection of the Claims pursuant to 35 U.S.C. section 102 was overcome by  
the present amendment

Claims 1 –9 and 28 – 32 were rejected as anticipated by U.S. Patent Application No. US 2004/0043044 (*Granger et al.*) This ground of the rejection was obviated by cancellation of Claims 1 – 9 and 28 – 32. In this regard it is noted that after this cancellation all remaining claims of the application, except for Claim 33 and 34, define the compounds having inhibitory effect on CP450RAI by chemical structure. The *Granger et al.* reference does not show these chemical structures.

Claim 33 is drawn to a compound which is an ester of retinol (a defined structure) with a compound having inhibitory effect on the enzyme CP450RAI. Again, the *Granger et al.* reference does not disclose this structure. Accordingly, the rejection for anticipation over this reference should be withdrawn in its entirety.

Regarding the rejection of claims pursuant to 35 U.S.C Section 112, second paragraph

Claims 17 – 23 were rejected because Claim 16 did not have the appropriate antecedent basis for the situation where the variable  $R_2$  is hydrogen. This ground of the rejection has been overcome by inserting “hydrogen” in the appropriate place. Similarly, “hydrogen” was also inserted into the definition of  $R_2$  in Claim 10. The specification was also amended on pages 23 and 24 regarding Formula A and Formula B by inserting “hydrogen” into the definition of the variable  $R_2$ .

The foregoing amendments of the specification and of Claims 10 and 16 do NOT constitute new matter for several reasons.

Regarding Formula A, the third line from the bottom of page 23 states that “preferably “ $R_2$  is H”, and originally filed Claim 14 shows a compound where  $R_2$  is in fact hydrogen.

Regarding Formula B, the fourth paragraph of page 25 states that in the preferred compound the aromatic portion of the chroman nucleus is substituted only by the variable Y in the 8 position and by the carbonyloxy-phenyl or ethynyl group in the 6 position. This means that in these preferred compounds  $R_2$  is hydrogen. Moreover, page 27 of the specification shows a number of actual preferred compounds where the variable  $R_2$  is indeed hydrogen, and originally filed Claims 18, 19 and 20 show the same thing.

Rejection of the claims for indefiniteness on the grounds that the terms “retinoid” and “a derivative of vitamin A having vitamin A like biological activity” are not adequately defined is respectfully traversed.

The term retinoid is well known and understood by those having ordinary skill in the art. This is amply demonstrated, for example, by a search of all United States patents issued since 1976 which have the term “retinoid” in their title. Applicant’s undersigned attorney performed such a search on the U.S Patent Office’ publicly available website and obtained 287 “records”. A print-out demonstrating this search is enclosed as Exhibit 1. An article titled “Current Use and Future Potential Role of Retinoids in Dermatology” in the scientific publication “Drugs 1997 Mar. 53(3) 358 – 388” is enclosed here as Exhibit 2. The Examiner’s attention is drawn to the definition of “retinoids” on page 359 of this review article where it is stated:

“ ‘Retinoids’ is a generic term that includes both naturally occurring molecules and also synthetic compounds showing specific biological activities resembling those of vitamin A (retinol).”

The just quoted statement and the further reading of this article proves without any doubt that the term “retinoid” as well as the term “a derivative of vitamin A having vitamin A like biological activity” are well defined and well understood by persons having ordinary skill in the art.

Moreover, it is respectfully submitted that the rejection for the allegedly inadequate definition of the terms “retinoid” or of “a derivative of vitamin A having vitamin A like biological activity” is *a priori* inapplicable to each outstanding claim of the application where the compound of category (2) is defined simply as “Vitamin A”. These claims are 11, 13, 15,

17, 20, and 23. Moreover, in Claim 33 the structure particularly shown is retinol so that the rejection for indefiniteness is cannot be applicable to this claim.

Still further, its is noted that Claims 15, 20, and 23 are drawn to a method using a combination of a single compound of defined structure with Vitamin A. Again, the rejection for indefiniteness *a priori* cannot be applicable to these claims.

Rejection of the method claims for lack of enabling disclosure is in error and should not be maintained

With regard to any possible or potential issue as to the adequate teaching of what is a “retinoid” or “a derivative of vitamin A having vitamin A like biological activity” the remarks regarding 35 U.S.C section 112, second paragraph are also applicable here.

With regard to the Office Action stating that the teaching is inadequate because the claims are drawn to a method of treating “any” disease it is noted that the claims in issue do not mention any specific disease. They are drawn to inhibiting the enzyme CP450RAI by administering an inhibitory compound of defined chemical structure (category 1) and at the same time administering a retinoid or Vitamin A or a compound having Vitamin A like biological activity (category 2). That the compounds of category 1 inhibit the enzyme CP450RAI is adequately demonstrated in the present specification.

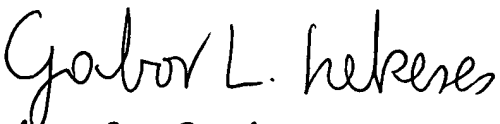
The law is well established that in order to evaluate patentability, assays, even in vitro assays, accepted in the state of the art are sufficient to provide an adequate disclosure provided the art considers the assay to be indicative of the ability or probability of the compounds to treat, ameliorate or prevent certain diseases and conditions. Thus, knowledge of the nature of

“retinoids”, knowledge and demonstrated ability of the compounds of this invention to inhibit the enzyme P450RAI which lessens the metabolic breakdown of retinoids in the body, are sufficient to enable the claims which call for inhibition of that enzyme without mentioning any specific disease but showing the structure of the specific inhibitor compounds. For the same reasons, methods using the *combination* of the compounds of the invention inhibiting the breakdown of “retinoids” with retinoids (and specifically with Vitamin A) are also enabled. A person of ordinary skill in the art the will be able to use, without undue experimentation, the methods of the invention in light of the present disclosure and knowledge of prior art.

In light of the foregoing, all outstanding claims of the present application are in *prima facie* allowable condition, and their early allowance is respectfully solicited.

In the event the Examiner is of the opinion that a telephone conference with the undersigned attorney would materially facilitate the final disposition of this case, she is respectfully requested to telephone the undersigned attorney at the below listed telephone number.

Respectfully submitted

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